

WE CLAIM:

1. A cell of the skin comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;
- b) a 3' splice region comprising a branch point and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell of the skin.

2. A cell of the skin comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;
- b) a 3' splice acceptor site;

- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell of the skin.

3 A cell of the skin comprising a nucleic acid molecule wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell of the skin.

4. The cell of claim 1 wherein the nucleic acid molecule further comprises a 5' donor site.

5. The cell of claim 1 wherein the 3' splice region further comprises a pyrimidine tract.
6. The cell of claim 1, 2 or 3 wherein said nucleic acid molecule further comprises a safety sequence comprising one or more complementary sequences that bind to one or both sides of the 5' splice site.
7. The cell of Claim 1, 2 or 3 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.
8. The cell of Claim 1 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.
9. The cell of Claim 1 wherein the nucleotide sequences to be *trans*-spliced to the target pre mRNA encodes a polypeptide expressed within the cell of the skin.

10. The cell of claim 9 wherein the polypeptide is a keratinocyte specific polypeptide.
11. The cell of claim 9 wherein the polypeptide is a melanocyte specific polypeptide.
12. The cell of Claim 9 wherein the polypeptide is selected from the group consisting of a plectin, type VII collagen, type XVII collagen, and laminin polypeptide.
13. The cell of claim 1 wherein said cell is a cancer cell of the skin.
14. The cell of claim 10 wherein said cell is a melanoma or basal cell carcinoma cell.
15. The cell of claim 1 wherein said cell is selected from the group consisting of a keratinocyte, melanocyte and dermal papilla cell.
16. A cell of the skin comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:
 - a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;

- b) a 3' splice region comprising a branch point and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell of the skin.

17. A cell of the skin comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell of the skin.

18. A cell of the skin comprising a recombinant vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell of the skin.

19. The cell of claim 16 wherein the nucleic acid molecule further comprises a 5' donor site.

20. The cell of claim 16 wherein the 3' splice region further comprises a pyrimidine tract.

21. The cell of Claim 16, 17 or 18 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

22. A method of producing a chimeric RNA molecule in a cell of the skin comprising:

contacting a target pre-mRNA expressed in the cell of the skin with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;
- b) a 3' splice region comprising a branch point and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell of the skin.

23. A method of producing a chimeric RNA molecule in a cell of the skin comprising:

contacting a target pre-mRNA expressed in the cell of the skin with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; under conditions in which a portion of the nucleic acid molecule is *trans*-spliced to a portion of the target pre-mRNA to form a chimeric RNA within the cell of the skin.

24. A method of producing a chimeric RNA molecule in a cell of the skin comprising:

contacting a target pre-mRNA expressed within the cell with a nucleic acid molecule recognized by nuclear splicing components wherein said nucleic acid molecule comprises:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within the cell of the skin;

- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

25. The method of claim 22 wherein the nucleic acid molecule further comprises a 5' donor site.

26. The method of claim 22 wherein the 3' splice region further comprises a pyrimidine tract.

27. The method of claim 22, 23, or 24 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

28. The method of Claim 22 wherein the nucleotide sequences to be *trans*-spliced to the target pre-mRNA encodes a polypeptide expressed within the cell of the skin.

29. The method of claim 28 wherein the polypeptide is a keratinocyte specific polypeptide.

30. The method of claim 28 wherein the polypeptide is a melanocyte specific polypeptide.

31. The method of Claim 28 wherein the polypeptide expressed within the cell of the skin is selected from the group consisting of a plectin, type VII collagen, type XVII collagen, and laminin polypeptide.

32. The method of claim 22 wherein said cell of the skin is a cancer cell.

33. The method of claim 32 wherein said cell is a melanoma or basal cell carcinoma cell.

34. The method of claim 32 wherein the nucleotide sequence to be trans-spliced to the target pre-mRNA encodes a polypeptide toxic or of therapeutic value to said cell.

35. The method of claim 22 wherein said cell is selected from the group consisting of a keratinocyte, melanocyte and dermal papilla cell.

36. A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin;
- b) a 3' splice region comprising a branch point and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain;and
- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

37. A nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain;and

- d) a nucleotide sequence to be trans-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

38. A nucleic acid molecule comprising :

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

39. The nucleic acid molecule of claim 36 wherein the nucleic acid molecule further comprises a 5' donor site.

40. The nucleic acid molecule of claim 36 wherein the 3' splice region further comprises a pyrimidine tract.

41. The nucleic acid molecule of claim 36, 37 or 38 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

42. The nucleic acid molecule of claim 36 wherein the binding of the nucleic acid molecule to the target pre-mRNA is mediated by complementary, triple helix formation, or protein-nucleic acid interaction.

43. The nucleic acid molecule of claim 36 wherein the nucleotide sequences to be trans-spliced to the target pre mRNA encodes a polypeptide expressed within a cell of the skin.

44. The nucleic acid molecule of claim 43 wherein the polypeptide is a keratinocyte specific polypeptide.

45. The nucleic acid molecule of claim 40 wherein the polypeptide is a melanocyte specific polypeptide.

46. The nucleic acid molecule of Claim 43 wherein the polypeptide expressed within the cell of the skin is selected from the group consisting of a plectin, type VII collagen, type XVII collagen, and laminin polypeptide.

47. The nucleic acid molecule of claim 36 wherein the nucleotide sequence to be *trans*-spliced to the target pre-mRNA encodes a polypeptide toxic or of therapeutic value to said cell.

48. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin;
- b) a 3' splice region comprising a branch point and a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA; wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell of the skin.

49. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin;
- b) a 3' splice acceptor site;
- c) a spacer region that separates the 3' splice region from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

50. A eukaryotic expression vector wherein said vector expresses a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin;
- b) a 5' splice site;
- c) a spacer region that separates the 5' splice site from the target binding domain; and
- d) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

51. The vector of claim 48 wherein the nucleic acid molecule further comprises a 5' donor site.

52. The vector of claim 48 wherein the nucleic acid molecule further comprises a pyrimidine tract.

53. The vector of claim 48, 49 or 50 wherein the nucleic acid molecule further comprises a safety nucleotide sequence comprising one or more complementary sequences that bind to one or more sides of the 3' splice region.

54. The vector of claim 48, 49 or 50 wherein said vector is a viral vector.

55. The vector of claim 44, 43 or 44 wherein expression of the nucleic acid molecule is controlled by a skin cell specific promoter.

56. A composition comprising a physiologically acceptable carrier and a nucleic acid molecule according to any of claims 36-47.

57. The composition of claim 56 wherein said composition is applied to the skin.

58. A method for correcting a genetic defect in a subject comprising administering to said subject a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin wherein said pre-mRNA is encoded by a gene containing a genetic defect; and
- b) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.

59. A method for imaging gene expression in a cell of the skin comprising administering to said subject a nucleic acid molecule comprising:

- a) one or more target binding domains that target binding of the nucleic acid molecule to a pre-mRNA expressed within a cell of the skin wherein said pre-mRNA is encoded by a gene containing a genetic defect; and
- b) a nucleotide sequence to be *trans*-spliced to the target pre-mRNA wherein said nucleotide sequence encodes a reporter molecule;

wherein said nucleic acid molecule is recognized by nuclear splicing components within the cell.